REMARKS

A. REQUEST FOR RECONSIDERATION

Applicants have carefully considered the matters raised by the Examiner in the outstanding Office Action dated August 27, 2007, but remain of the opinion that patentable subject matter is present. Applicants respectfully request reconsideration of the Examiner's position based on the amendments to the claims and the following remarks.

B. THE INVENTION

The present invention is directed to a pharmaceutical composition comprising a combination of formoterol and a steroidal anti-inflammatory agent.

One of the novel aspects of the invention is that the composition is stable for long term storage at a concentration suitable for direct administration. In the claimed composition, the formoterol is in solution, the steroidal anti-inflammatory is in suspension and the water is propellant-free. Additionally, the concentration of the formoterol in the composition is no greater than 200 μg/mL. These aspects are not taught or suggested in the prior art. Applicants therefore submit that these novel aspects of the present invention define over the references.

C. STATUS OF THE CLAIMS

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 are presented for further prosecution.

D. CLAIM OBJECTION AND AMENDMENT

The Examiner objected to claim 123 for containing a typographical error. Claim 123 has been amended to recite "dihydrate". Applicants respectfully submit that the amended claim is acceptable.

E. PRIOR ART REJECTIONS

The Examiner has made the following four obviousness rejections under 35 U.S.C. §103:

(1) Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 99-112, 117-119 and 122-128 are unpatentable over Hochrainer et al. (U.S. 6,150,418) in view of Carling et al. (U.S. 5,674,860) and PDR;

(2) Claim 93 is unpatentable over Hochrainer in view of Carling and PDR, and further in view of PDR, pages 482, 535, 537 and 2828;

(3) Claims 113-116 and 120-121 are unpatentable over Hochrainer in view of Carling and PDR, and further in view of Hardman et al. (Goodman Gilman's *The Pharmacological Basis of Therapeutics*, 1996, page 665) or Leckie et al. (*Novel Therapy of COPD*, abstract, Jan 2000); and

(4) Claims 129-146 are unpatentable over Hochrainer in view of Remington's Pharmaceutical Sciences, Seventeenth Edition, 1985, pages 1443 and 1451.

It is noted that the references cited above, with the exception of Remington's Pharmaceutical Sciences, had also been cited in the previous Office Action dated March 13, 2007. At the outset, the undersigned hereby incorporates by reference, all remarks made in the last response made of record by the Examiner.

Hochrainer had been cited to teach aqueous compositions containing formoterol, with the formoterol in solution, and suitable for long term storage. Applicants submit that Hochrainer does not teach a composition that is suitable for long term storage and administration without dilution (col. 4, lines 9-13). In fact, on page 13 of the Office Action, the Examiner had stated that Hochrainer "teaches that the composition disclosed therein need to be diluted before use" (emphasis added). Thus, Hochrainer explicitly teaches that the active substance concentrates that are suitable for long term storage are not also suitable for direct administration. Hochrainer also does not teach any particular steroid or pharmaceutical composition having formoterol in solution and a steroidal anti-inflammatory agent in suspension. Rather, Hochrainer teaches that formoterol can be in solution or in suspension (Abstract), and actually teaches away from the present invention because he teaches that "[formoterol] suspensions are preferred as they have proved particularly stable on storage" (col. 1, lines 66-67). Moreover, Hochrainer also does not teach or suggest teach or suggest dilute aqueous pharmaceutical compositions comprising formoterol and a steroid, wherein the formoterol concentration is no greater than 200 µg/mL. In

fact, the lowest formoterol concentration disclosed in Hochrainer is 900 μg/mL, which is almost 5 times more concentrated than the claimed concentration in the present application. Furthermore, formulations of Hochrainer with formoterol in a concentration of 900 μg/mL are for administration, not for long term storage (col. 3, line 66-col. 4, line 28). Thus, Hochrainer actually teaches away from the present invention since Hochrainer teaches that compositions containing 900 μg/mL would not be stable for long term storage.

The Examiner recognized that Hochrainer does not teach (1) dilute compositions that are suitable for long-term storage and direct administration (page 13 of the Office Action), (2) compositions with steroid in suspension in propellant-free water (page 5 of the Office Action), and (3) compositions having at most 200 μg/mL of formoterol (page 5 of the Office Action). The Examiner cited Carling, PDR, Hardman, Leckie and Remington's Pharmaceutical Services to teach these elements. Applicants respectfully submit that Hochrainer, alone and in combination with any or all of the secondary references, does not teach pharmaceutical compositions of the present invention.

The Examiner's attention is drawn to commonly assigned U.S. Patent Nos. 6,667,344 and 6,814,953, which both claim the benefit of priority from U.S. Provisional Patent Application Serial No. 60/284,606 filed April 17, 2001, the same priority date as the present application. The claimed formoterol containing compositions suitable for long term storage and direct administration recited in the '344 patent and the '953 patent were found by the USPTO to be patentable over Hochrainer and the PDR, which have also been relied upon in the present application. The claim language relating to formoterol in the independent claims of the present application conforms to the compositions comprising formoterol claimed in the '344 patent and the '953 patent. The USPTO has repeatedly confirmed that these types of formoterol containing compositions are novel. The ineluctable conclusion is that the present application, entitled to the same priority date as the '344 and the '953 patents is also patentable over the same Hochrainer-based combinations. Moreover, the Examiner's attention is also directed to commonly assigned U.S. Patent Application Serial No. 10/887,785 which claims the benefit of priority from U.S. Provisional Patent Application Serial No. 60/486,386 filed July 10, 2003, and was recently issued a Notice of Allowance on January 15, 2008. The claimed formoterol containing unit doses suitable for long term storage recited in the '785 application were also deemed patentable

over Hochrainer by the USPTO. Thus, the claims presented in the present application, which are entitled to an earlier priority date than the '785 application, should also be deemed patentable.

Those references which failed to disclose the proper formoterol compositions in the '344 patent, the '953 patent and the '785 application surely cannot be any more relevant to claims directed to formoterol and steroid combinations. Thus, one difference between the presently claimed invention and the inventions claimed in the '344 patent, the '953 patent and the '785 application is that the claims herein also include a steroid. As will be shown below, none of the additional references cited by the Examiner in the present case teach or disclose the dilute aqueous formulations of formoterol in solution and steroid in suspension suitable for long-term storage and direct administration.

The Examiner cited Carling to teach the combination of formoterol and steroid. However, Carling does not teach dilute aqueous pharmaceutical compositions with formoterol in solution and steroid in suspension in water that is propellant-free, that are suitable for long-term storage and direct administration. The Examiner cited column 4, lines 12-14 of Carling to teach improving physical stability of a mixture. However, this passage does not describe the stability of the composition, only that excipients can be added to increase stability of the mixture. Furthermore, the passage cited by the Examiner teaches a micronized mixture of formoterol and steroid, with both in suspension in liquid propellant. This is not the formulation of the present invention. The claims require an aqueous formulation of formoterol in solution and a steroidal anti-inflammatory agent in suspension, in propellant-free water. Thus, Carling does not cure the deficiencies of Hochrainer.

The Examiner cited the PDR to teach the use of steroids for treating asthma. Applicants do not deny that steroids are useful in the treatment of asthma. However, the PDR does not teach pharmaceutical compositions comprising formoterol in dilute solution and steroid in suspension, in propellant-free water, which is suitable for long term storage and direct administration. Thus, the PDR does not cure the deficiencies of Hochrainer and Carling.

Applicants note that on page 7 of the Office Action, the Examiner states "it is noted that fluticasone is not water soluble, therefore a suspension of fluticasone would have been obvious to one of ordinary skill in the art." However none of the references cited by the Examiner teach formoterol in solution and steroid in suspension, in propellant-free water. Nor do any of the references cited by the Examiner teach that such a composition would be stable for long term

storage and suitable for direct administration without dilution. In contrast, the present invention requires formoterol to be in solution, and steroidal anti-inflammatory to be in suspension. Typically, formulations having one drug in solution and one drug in suspension are not stable. To accept the Examiner's position regarding the combination would therefore require impermissible hindsight. Thus, in order to obtain a stable formulation, typically both drugs are provided either in suspension or in solution. Therefore, it is unexpected that formulations of the present invention are stable for long-term storage and direct administration as is claimed in the present application.

Moreover, the deficiencies of Hochrainer, Carling and the PDR are not cured by Hardman, Leckie and Remington's Pharmaceutical Sciences. Hardman, Leckie and Remington's Pharmaceutical Sciences do not disclose compositions with formoterol and steroid in propellant-free water that are suitable for long-term storage and direct administration without dilution. Thus, the secondary references in combination with Hochrainer, Carling and the PDR neither teach nor suggest the pharmaceutical compositions of the present invention.

Since none of the references cited by the Examiner in combination with Hochrainer teach or suggest a dilute aqueous pharmaceutical compositions comprising formoterol in solution and steroid in suspension, in propellant-free water, and where the dilute aqueous solutions are suitable for both long term storage and direct administration, it is respectfully submitted that the combination of the references cited by the Examiner would not have led one of ordinary skill in the art to the claimed invention. Thus, applicants submit that the claims presented herein are patentable over the Examiner's rejections which are based principally upon Hochrainer.

F. **FEES**

A three-month extension of time is hereby requested and the extension of time fee is hereby paid along with the online filing. If it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to deposit account 02-2275. Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

Respectfully submitted,

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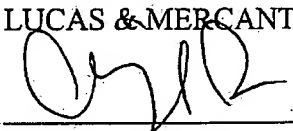

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